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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,798	08/25/2003	Anurag Rathore	161765.00520	3621

28523 7590 12/07/2007

PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
EASTERN POINT ROAD
GROTON, CT 06340

EXAMINER
GUDIBANDE, SATYANARAYAN R

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
12/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/646,798	RATHORE ET AL.	
	Examiner	Art Unit	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34 and 39-76* is/are pending in the application.

4a) Of the above claim(s) *69-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34, 39-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I invention in the reply filed on October 3, 2005 is acknowledged. The traversal arguments were addressed in the non-final rejection dated 11/29/05.

Applicants remarks in the response filed on 9/30/07 have been acknowledged.

Claims 1-34 and 39-76 are pending.

Claims 69-76 have been withdrawn from further consideration as being drawn to non-elected invention.

Claims 1-34 and 39-68 are examined on the merit.

Any objections and rejections made in the previous office action dated 6/28/07 and not specifically mentioned here are considered withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the

various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-68 remain rejected under 35 U.S.C. 1.03(a) as being unpatentable over US patent 5,849,535 issued to Cunningham, in view of Jespersen, et al., Eur. J. Biochem., 1994, 219, 365- 373, and further in view of Houk, et al., J. Am Chem. Soc., 1987, 109, 6825-6836 as stated in our non-final office action dated 6/28/07.

Applicants argue that the combination of references, Cunningham, et al., Jespersen, et al., and Houk, et al., fail to provide teachings to provide the instant invention obvious to one skilled in the art the use of a mercapto compound to decrease the amount of a trisulfide isoform impurity produced in a recombinant production process for a growth hormone antagonist polypeptide.

Applicants acknowledge that Jespersen, et al., teaches the characterization of a trisulfide derivative of human growth hormone produced in E. Coli and submit that 1,4-dithiothretol and cysteine were only used to characterize the novel protein derivative and does not teach a method as presently claimed for reducing the amounts of impurities in the recombinant production of growth hormone or even suggest that the reagents used to characterize the protein derivative should be included in a recombinant manufacturing process to decrease the amount of this impurity.

Applicants further argue that there is no teaching or suggestion to use the teachings of Houk, et al., in combination with Cunningham and Jespersen for reducing the trisulfide isoform of human growth hormone in a recombinant suspension of human growth hormone.

Applicant's arguments filed on 9/21/07 have been fully considered but they are not persuasive. Because, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, contrary to applicants argument that "Jespersen, et al., teaches the characterization of a trisulfide derivative of human growth hormone produced in E. Coli and submit that 1,4-dithiothretol and cysteine were only used to characterize the novel protein derivative and does not teach a method as presently claimed for reducing the amounts of impurities in the recombinant production of growth hormone or even suggest that the reagents used to characterize the protein derivative should be included in a recombinant manufacturing process to decrease the amount of this impurity". The following paragraph from the Jespersen, et al., on page 365, column 2, the cited reference recognizes that there was a problem in the purification of the recombinantly produced growth hormone in E. coli., in the form a hydrophobic derivative that separated from the native BhGH which is a trisulfide impurity and the

Jespersen, et al., were able to characterize this trisulfide impurity with the help of reducing agent 1,4-dithiothreitol and cysteine. The reference also teaches that the 1,4-dithiothreitol was added in-situ prior to sample preparation and analysis by mass spectroscopy (page 367, column 1, paragraph 2). Therefore, the problem of the presence of the trisulfide impurity was well known to Jespersen, et al., and they were successful in finding a solution to reduce the impurity in situ as stated above.

E. coli cells transformed with a plasmid designed for expression of amino-extended BhGH intracellularly have been shown to result in formation of the correct disulphide bonds after extraction and processing [14]. However, there are some indications that the disulphide bond between Cys182 and Cys189 (minor loop) shows decreased stability relative to the bond between Cys54 and Cys165 (major loop) due to its position at the surface of the molecule [15]. In connection with process development of BhGH, it was observed that a hydrophobic derivative was separated from the native BhGH during the step using hydrophobic interaction chromatography (HIC). A closer investigation by means of peptide mapping, HIC, mass spectrometry (MS) and detection of sulphur liberation showed that the hydrophobic BhGH-related product was a BhGH derivative in which a trisulphide bond was formed between Cys182 and Cys189. This paper emphasizes the characterisation and procedures for renaturation of this trisulphide derivative of BhGH (BhGH*) produced in *E. coli* cells.

The reference of Houk, et al., has been used to support the fact the functional equivalents of the compounds recited in the instant application can be used individually or in combinations of others for the purpose of reducing the disulfide and trisulfide linkages as stated in the office action dated 6/28/07 on page 4.

Therefore, the combination of the cited references Cunningham, Jespersen and Houk, is proper in maintaining the rejection under obviousness as stated in the previous office action dated 6/28/07.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

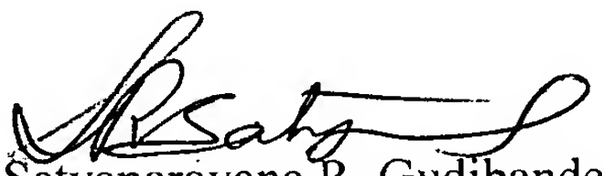
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Satyanarayana R. Gudibande, Ph.D.
Art Unit 1654